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## PERIOSTITIS OF THE RIBS AFTER TYPHOID FEVER,

AND ITS PROBABLE DEPENDENCE ON MEDICATION.

A clinical lecture delivered at Cooper Medical College, San Francisco, by

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*Gentlemen:*—It is an established dogma in medicine that periostitis of the long bones may occasionally occur as a sequel of typhoid and other exhausting fevers.<sup>1</sup> Arising thus, it is most prone to affect the tibia, but has been observed upon the ribs in a few cases. Instances of the latter occurrence are extremely rare. During the War of the Rebellion, nearly 80,000 cases of typhoid fever occurred in the Union army, and form the subject of the voluminous report thereon in the third volume of the Medical History of that War. Yet, on page 476 of this volume, we find the following remarks:

"There is no instance of disease of the bones following continued fever to be found among the post-mortem records, although the clinical accounts of severe rheumatic pain endured by convalescents render it probable that the periosteum and bones occasionally became affected, and that the large burrowing abscesses sometimes observed were associated with caries or necrosis."

In a foot-note appended to this paragraph, the writer refers to Prof. W. W. Keen's Toner Lecture No. 5, and to Sir James Paget's paper in St. Bartholomew's Hospital Reports, vol. xii, 1876, for further information on this subject. I wrote to the Smithsonian Institution for the former, and to London for the latter, and find that Dr. Keen, in his able lecture on the "Surgical Complications and Sequels of the Continued Fevers," for which he made a special study of the subject, and in which he refers to a most exhaustive list of authorities, does not mention periostitis of the ribs, though referring to sixty-nine cases of

<sup>1</sup>Heath's Dict. of Surgery, vol. ii, page 193. Quain's Dict. of Med., p. 125.





diseases of bone following continued fevers, of which three were of periostitis, and fifty of necrosis. Of these twenty-two involved the head, seven the trunk, six the upper extremities and forty-two the lower.

That periostitis of the ribs may, however, occur in connection with typhoid fever, is clearly shown by Sir James Paget in the paper referred to. As his is the only description of the affection to be found, I will read to you what he says on the subject, in full.

“The periostitis following typhoid fever has its most frequent seat on the tibiæ, but I have seen it on the femur, the ulna, the parietal bone. \* \* \* The periostitis of the ribs is so much unlike the kind just described, that I have never yet seen it associated with necrosis. It so nearly resembles the ordinary scrofulous periostitis of ribs, that I have sometimes thought it should be regarded too as only an evidence of scrofula educed by the feebleness of nutrition consequent on the fever. Yet I have never seen it associated with other similar signs of scrofula, and it has occurred, after typhoid, in some of so robust and apparently unblemished constitution, that it would seem absurd to impute scrofula to them.

“In the usual course of this disease, beginning always, I believe, in the convalescence, a well-defined round or oval swelling is found on one or more ribs. Whether on bone or cartilage, the swelling is generally on the front of the chest. It is painful and tender, and suppuration slowly ensues in it. Then slowly it discharges itself through one or more channels, leading obliquely through the overlying structures and through small openings in the skin. The flow of pus, thin and pale, continues usually for many months; I have known it continue for even two years; and not rarely fresh openings are formed for branches from the first channel of discharge. In the end complete healing takes place, with deep depressed scars, and complete clearing up of all the periosteal swelling.

“I have never known necrosis of a rib in these cases, nor ever seen or heard of any advantage from laying wide open any of the sinuses. The general health never appears to be seriously affected by the abscesses, unless in persons of naturally feeble health. Commonly, indeed, the patients feel quite well, and can be active, suffering nothing more than slight local inconvenience.

“All the cases of this sequel of typhoid fever that I have seen have been singularly alike, varying only in the position of the abscess. In one, in which I believe that the disease began in the periosteum of the eleventh or twelfth rib, a great abscess slowly made its way between the abdominal muscles, and I had to open it at the groin. In that case alone have I seen life endangered.” (St. Bartholomew's Hospital Reports, vol. xii, 1876, p. 3.)

NOTE.—In a recent letter from patient No. 1, he says that antifebrin was prescribed on October 6, in 15-grain doses, and was continued twice daily throughout the entire illness—part of the time reduced to  $7\frac{1}{2}$  grains.



Strumpel (*Prac. of Med.*, p. 16) says:

"Lesions of the bones and joints occur but seldom. We have seen periostitis of the tibia and of a rib, during convalescence. Swelling of the joints is equally rare."

MacCormac (*Quain's Dict. of Med.*, p. 125) says:

"A peculiar form of chronic periostitis is occasionally observed as a sequel to typhoid fever. It occurs during convalescence, and without general symptoms. It takes the form of hot, painful and tender nodes, frequently symmetrical, and often placed on the tibia; the disease is also found on the ribs and other bones."

Gross does not mention typhoid fever in connection with periostitis, though he does ascribe it to gout, rheumatism and syphilis.<sup>1</sup> Neither does he refer to it as the cause of caries or necrosis of the ribs.<sup>2</sup> Holmes<sup>3</sup> is equally silent upon both subjects. None of the cases of excision of the ribs, mentioned in the *Surgical History of the War*, were ascribed to fever.<sup>4</sup> None of the regular text-books mention this affection, except in such general terms as include caries and necrosis of bone, gangrene of soft parts, etc.

It will now be evident to you all that the simultaneous occurrence of two cases of so rare a sequel of so common a disease as typhoid fever, in the same town, and under the same treatment, would direct attention to the treatment, with the object of ascertaining whether or not this had anything to do with the causation. Such cases I have had brought to my notice, and now bring before yours.

(1.) Mr. J. F. A., a druggist, residing in an interior city, was taken down with typhoid fever last October. The fever pursued its usual course, without any particularly marked complications. There was no delirium, no hemorrhage, no perforation. Large doses of antifebrin were employed, averaging seven and one half grains several times daily, for over a month. He was out of bed November 10th, and from that time, he writes, he "was up and around more or less every day, but had all the time severe pain in the region where the tumors afterwards came, and was treated for rheumatism by salol. The pain kept up, and has ever since." In December, about the first of the month, a tender swelling appeared over the sternum, followed by

<sup>1</sup>System of Surgery, 6th ed., vol. i, p. 835. <sup>2</sup>Vol. ii, p. 1072.

<sup>3</sup>A System of Surgery, edited by T. Holmes, 1882.

<sup>4</sup>Medical and Surgical History of the War, Part I, vol. ii, p. 566.

another below the left nipple, and this by a third over the third right rib, and a fourth over the seventh and eight left ribs, as well as a fifth over the fifth right rib. All occurred on the front of the chest, and appeared during the months of December, January and February. The third and fourth did not go on to maturity, the former disappearing after a time, and the latter remaining tender and swollen, to this date. The other three ran a peculiar course. At first tender to the touch, they soon became of a bluish-red color, and when opened, as they were by the knife, discharged nothing but blood. One of these swellings was opened by myself in May last, when the patient first consulted me. No pus appeared, but there escaped about a teaspoonful of dark blood, from a sinus in the tissues which reached down to the rib. The tissues in the immediate vicinity of the sinus were softened and gangrenous in appearance. The other two swellings had been opened before I saw the case, but a sinus remained open over each of them, which was partially filled with exuberant granulation-tissue, and on inserting a probe into them it went down to periosteum in one case, in the other striking bone, which felt perfectly smooth. I had intended laying these sinuses open, and placed the patient under an anæsthetic, for that purpose; but as he developed alarming symptoms, I desisted from any further operative measures, and took him to Professor Lane for consultation. Dr. Lane advised against any cutting operation, and cauterized each sinus several times with caustic potassa. I placed him from the commencement upon the iodide of iron and manganese, alternated with the tincture of the chloride of iron. He had previously taken large doses of potassium iodide for some time without result. In a month after coming to this city he had gained some fourteen pounds in weight, was eating and sleeping well, and was in excellent health, except for the open sinuses. After his return home in June I heard from him several times. In his last letter dated September 13th, he says "my general health is good, eat and sleep all right, but gain but little strength. The lower lump is about the same as when you saw it; the others about the same as when I came over to you, and some days so painful. The only work I do is my writing; am not strong enough to do much of anything else. Have'nt lost my nip, all the same; and hope to come out all right, yet."

(2.) Rev'd Mr. A. was taken down with typhoid fever about



the same time as the preceding case, in the same city, and was under the same treatment. When convalescence began, a similar state of affairs developed, in the form of one large swelling over the ribs, with great pain and soreness. He had also received large doses of antifebrin during the fever, and for several weeks duration. He went east, and in a Baltimore hospital was operated on for necrosis of the rib, a piece of the bone being excised. He returned to hospital for a second exsection, and about September 1st entered the hospital a third time for another operation. I cannot give the details of this case, as my information comes second-hand, through the first-named patient, who is a personal friend of the second, and has kept in correspondence with him throughout.

(3.) Mr. H. had typhoid fever in Montana, in the fall of last year; developed a large, tender swelling over the left lower ribs, soon after entering on convalescence. This was operated upon several times, pieces of necrosed bone being removed each time. The wound is now closing. The patient does not know the details of his treatment, and I have been unable to obtain them. He says, however, that he took a small, white powder, several times a day, for several weeks, while in the fever. Some of you have seen this patient frequently, and heard his story from his own lips. In fact, my attention was drawn to the case by a member of the class.

Authorities all agree that the periosteal inflammation following typhoid fever is due to the impaired condition of the blood produced by the disease. If, then, we still further lower the vitality of blood, by administering large doses of blood-injuring agents for a long period of time, we must increase the liability to such affections in any particular case. This is what I believe has occurred in these three instances.

At a meeting of the New York Pathological Society<sup>1</sup> Dr. Porter presented the liver and kidneys of a patient to whom large doses of antipyrin and antifebrin had been given, in which, as a result of the action of said drugs, it was thought, extensive fatty and granular metamorphosis had taken place. He said that the observation had been made that cases treated with these antipyretics recovered less quickly, *especially patients with typhoid fever*, the duration of the disease being then about forty-

<sup>1</sup>*N. Y. Med. Jour.*, July 30, 1887.

two days, as against an average of thirty-two days under other methods.

The long-continued administration of antifebrin, may, according to Herczel, lend to anilin anæmia or cachexia, with solution and decomposition of the coloring-matter of the blood.<sup>1</sup> Henocque observed that a change of the hemoglobin into methemoglobin takes place, having occurred in a man taking fifteen to eighteen grains daily, and the same thing has been noted by Fischer. The red corpuscles are altered in form, and perhaps in part dissolved, and the amœboid movements of the white corpuscles are stopped by this drug. These observations are confirmed by Ott, Bokai, and Lepine.<sup>2</sup> "It seems probable," says Prof. Wood, "that when the heart's action is already weak, ordinary medicinal doses may have a powerfully depressing effect: Biro saw seven and one-half grains cause weak, irregular pulse."<sup>3</sup>

Prof. Germain See pronounces antifebrin to be "a dangerous remedy," which, "from its toxic influence, should be discarded, —the patients becoming cyanosed, the oxyhemoglobin of the blood being transformed into metahemoglobin, and the respiratory faculty of this liquid is arrested. There is, therefore, no advantage in subjecting the patient to such dangers."<sup>4</sup> Prof. See criticises his illustrious confrere, Dujardin-Beaumetz, for using it too freely; and, commenting thereon, Dr. Humphreys says that the untoward effect of antifebrin on the blood has made him "somewhat cautious in its use here, where the malarial infection itself is too prone to produce hemoglobinuria, without the aid of a drug whose tendency is to precipitate such an undesirable result."<sup>5</sup>

Hemoglobin, the coloring matter of the red blood corpuscles, readily combines with oxygen to form an unstable and loose chemical compound, oxyhemoglobin; and this oxygen it gives up readily to the tissues. It may also form methemoglobin, which contains the same amount of oxygen, but in a different chemical union, while the oxygen is more firmly united with it. Methemoglobin is only formed from solutions of hemoglobin, and not within the blood corpuscles. It is produced spontaneously in old brown blood stains, in the crusts of bloody wounds, in blood cysts and

<sup>1</sup>*Ther. Gaz.*, Aug., 1888, p. 566.

<sup>2</sup>*Op. cit.*, p. 568. <sup>3</sup>*Op. cit.*, p. 569.

<sup>4</sup>*N.Y. Med. Rec.*, Oct. 8, 1887, p. 500. <sup>5</sup>*Ther. Gaz.*, July, 1889, p. 453.



in bloody urine (Landois). We have seen that antifebrin also produces this transformation. Hemoglobinuria is produced when hemoglobin occurs free within the blood vessels, as where the colored blood corpuscles have been dissolved inside the blood vessels. It also occurs in cases of severe burns, in pyæmia, scurvy, purpura, severe typhus, etc, and after the passage of pyrogallie acid, potassic chlorate, chloral, phosphorus or carbolic acid into the circulation (Landois). The presence of a large quantity of dissolved hemoglobin may cause extensive coagulation within the blood vessels (Francken). Dissolved hemoglobin seems greatly to increase the activity of the fibrin ferment. In septic fever the amount of ferment in blood may increase to such an extent as to permit the occurrence of spontaneous coagulation (thrombosis). In febrile cases, generally, the amount of ferment is more abundant (Landois). Two causes for such necroses and other forms of disease, such as periostitis and caries, in typhoid fever, are to be found; first, thrombosis and in some cases embolism; and secondly, absolute inanition or want of nutrition (Keen) .

From this brief resumé you will see how antifebrin can promote the liability to disease of the periosteum in such an exhausting and blood-impairing affection as typhoid fever. Whether it was responsible for this occurrence in the cases adduced, or not, is a subject for discussion; but, in my judgment, it must be credited with what otherwise would have been a most improbable occurrence, namely, the simultaneous appearance of two cases (probably three) of so rare a complication *under the same treatment*, two being in the same locality.

As to final treatment, resection of the rib is condemned by authority, and the result in two of the cited cases fully confirms Dr. Lane's prediction, that it meant repeated excision, until both patient and surgeon are worn out, and the whole rib finally removed. Holmes says that "the partial resections of the ribs, which have been chiefly practiced in Germany, do not seem very promising operations, while they are by no means free from difficulty and danger."<sup>1</sup> In Sir James Paget's experience, the sinuses always closed, in the end, and no mention is made by him of surgical interference.

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<sup>1</sup>System of Surgery, vol. iii, p. 196.



